S/N: 10/708,356

## IN THE CLAIMS

1. (Original) A method of clinical imaging comprising:

exciting water-exchangeable spins in oxygen-hearing molecules in a region-of-interest (ROI) having a change in oxygen status;

detecting proton transfer within the ROI from exchangeable protons within water; and

determining changes in oxygen levels across the ROI.

- 2. (Original) The method of claim 1 further comprising irradiating the ROI with exchangeable resonances and wherein the exchangeable resonances are within a resonance in a proton spectrum of one of deoxy-hemoglobin and dexoy-myoglobin.
- 3. (Original) The method of claim 2 further comprising selectively irradiating the ROI and distinguishing water signal changes within the ROI due to deoxy-hemoglobin and or deoxy-myoglobin from background MT effects.
- 4. (Amended) The method of claim 3 wherein the proton spectrum is within at least one of a range of approximately [[-]]10 to 80 ppm.
- 5. (Original) The method of claim 1 wherein exciting includes irradiating the ROI such that spins of at least one of deoxy-hemoglobin and deoxy-myoglobin is excited.
- 6. (Original) The method of claim 1 further comprising assessing oxygen depletion within the ROI.
- 7. (Original) The method of claim 1 further comprising acquiring MR imaging data from the directly imageable molecules via proton transfer to enhance contrast between oxygen-rich and oxygen-depleted tissue in the ROI.
- 8. (Original) The method of claim 1 further comprising acquiring spectral data to perform a spectral analysis of oxygen content within the ROI.

S/N: 10/708,356

- 9. (Original) The method of claim 1 further comprising mapping the oxygen levels across the ROI.
- 10. (Original) A method of determining oxygenation of heme-proteins in vivo comprising:

applying radio frequency (RF) energy to an imaging subject to excite offresonance spins of water-exchangeable molecules;

determining proton transfer from excited water-exchangeable molecules to non-excited molecules;

acquiring MR data from the non-excited molecules; and determining oxygen content of the water-exchangeable molecules from the MR data.

- 11. (Original) The method of claim 10 further comprising determining a concentration of at least one of deoxy-hemoglobin and deoxy-myoglobin in the imaging subject.
- 12. (Original) The method of claim 10 further comprising determining a spatial distribution of oxygen debt across a data acquisition region.
- 13. (Original) The method of claim 10 further comprising determining proton transfer from the water-exchangeable molecules to water molecules.
- 14. (Original) The method of claim 10 wherein applying RF energy further comprises applying off-resonance RF pulses.
- 15. (Original) The method of claim 10 wherein applying RF energy further comprises applying a paramagnetic hyperfine-shifted exchangeable resonance RF pulse sequence to the imaging subject.

S/N: 10/708,356

16. (Original) A magnetic resonance imaging (MRI) apparatus comprising:

an MRI system having a plurality of gradient coils positioned about a bore of a magnet to impress a polarizing magnetic field and an RF transceiver system and an RF switch controlled by a pulse module to transmit RF signals to an RF coil assembly to acquire MR images; and

a computer programmed to:

cause application of a pulse sequence to excite oxygen-bearing molecules within a ROI having a change in oxygenation;

acquire MR data from directly imageable molecules having been influenced by the oxygen-bearing molecules; and

reconstruct an image from the MR data to illustrate a change in oxygen debt across the ROI.

- 17. (Original) The MRI apparatus of claim 16 wherein the oxygen-bearing molecules include deoxy-heme-proteins.
- 18. (Original) The MRI apparatus of claim 17 wherein the deoxy-heme-proteins include at least one of deoxy-hemoglobin and deoxy-myoglobin.
- 19. (Original) The MRI apparatus of claim 16 wherein the oxygen-bearing molecules include proximal histidine NH.
- 20. (Original) The MRI apparatus of claim 16 wherein the computer is further programmed to determine oxygen concentration across the ROI.
- 21. (Original) The MRI apparatus of claim 16 wherein the computer is further programmed to map oxygenation levels across the ROI.
- 22. (Original) The MRI apparatus of claim 16 wherein the RF pulse sequence is configured to excite the oxygen-bearing molecules to a saturation such that a water transfer effect excites the directly imageable molecules.

S/N: 10/708,356

- 23. (Original) The apparatus of claim 16 wherein the computer is further programmed to cause the ROI to be irradiated with multiple exchangeable resonance frequencies to enhance resolution of the image.
- 24. (Original) The apparatus of claim 16 wherein the computer is further programmed to cause the ROI to be irradiated with multiple exchangeable resonance frequencies substantially simultaneously.
- 25. (Original) A system of oxygen content determination comprising:

  means for exciting spins limited to targeted oxygen-carrier molecules;

  means for determining a proton transfer from the targeted oxygen-carrier

  molecules to imageable molecules; and

means for determining oxygenation of the targeted oxygen-carrier molecules from a reconstructed image of the imageable molecules.

- 26. (Original) The system of claim 25 further comprising means for limiting spin excitation to proximal histidine NH molecules in an ROI.
- 27. (Original) The system of claim 25 further comprising means for displaying a spatial distribution of oxygen depletion across the ROI.
- 28. (Original) The system of claim 25 further comprising means for determining a concentration of at least one of deoxy-hemoglobin and deoxy-myoglobin in the ROI.
- 29. (Original) The system of claim 25 further comprising means for determining cancerous tissue presence in an ROI.
- 30. (Original) The system of claim 25 further comprising means for localizing oxygen depletion across an ROI.